Histologic variants (tall cell, columnar cell, diffuse sclerosing) of papillary thyroid cancer (PTC) have a worse prognosis, as do more invasive variants of follicular type. Intermediate risk of recurrence includes (1) microscopic invasion of tumor into the perithyroidal soft tissues, (2) cervical lymph node metastases, (3) $^{131}$I uptake outside the thyroid bed, (4) aggressive histology, or (5) intrathyroidal vascular invasion. High-risk of recurrence includes (1) gross tumor invasion, (2) incomplete tumor resection, (3) distant metastases, and possibly (4) elevated thyroglobulin unexplained by uptake on posttreatment $^{131}$I scan. Postoperative $^{131}$I remnant ablation facilitates the early detection of recurrence based on serum Tg measurement and/or $^{131}$I; in addition, the post-therapy scan identifies previously undiagnosed disease, especially in the lateral neck. Furthermore, this first dose of I-131 eliminates any thyroid cancer cells remaining after surgery in patients at risk for recurrence or disease-specific mortality. I-131 ablation is recommended for all patients with distant metastases, gross extrathyroidal extension, or primary tumor size >4 cm. For 1- to 4-cm thyroid cancers confined to the thyroid with lymph node metastases or other higher-risk features, I-131 ablation is not recommended for primary tumors <1 cm, even if multifocal. Children achieve the adequate TSH elevation by 2 weeks of Synthroid withdrawal. For patients being prepared for ablation by hormone withdrawal, T4 may be resumed on the second or third day after $^{131}$I therapy. Thyrogen was approved for preparation of ablation in December 2007, and this approach is "strongly recommended" by the new ATA guidelines. What activity of $^{131}$I should be used for remnant ablation? A recent prospective, randomized study found no significant difference in the remnant ablation rate using 30 or 100 mCi of I-131. However, if residual microscopic disease is suspected, or if there is a more aggressive tumor histology (eg, tall cell, insular, columnar cell carcinoma), then higher activities (100 to 200 mCi) are appropriate. Low-iodine diets (<50 μg/day) increase the effective radiation dose. A low-iodine diet for 1 to 2 weeks is recommended for patients undergoing I-131 remnant ablation. Post-therapy whole-body iodine scanning conducted approximately 1 week after I-131 therapy visualizes additional metastatic foci in 10% to 26% of patients compared with the diagnostic scan. Look for new abnormal uptake in the neck, lungs, and mediastinum.

**Reviewer's Comments:** New developments are being reported, particularly in the detection of molecular and genetic markers, which the guidelines acknowledge without a specific recommendation. While the published guidelines provide education as well as clinical advice, the best advice is to keep current. I wonder whether the ATA will have to publish another sooner-than-expected update to its guidelines in the next couple of years. The current guidelines are printed in the November 2009 issue of *Thyroid*. (Reviewer-).
The addition of SPECT/CT to both SPECT and planar bone imaging leads to improved diagnostic confidence for the presence or absence of metastases.

**Background:** SPECT/CT is gaining favor as the preferred method for evaluating patients for skeletal metastases with Tc-99m MDP. Using co-registration with CT, it is possible to better determine if a lesion is located in the pedicle (and very likely metastatic) or located in the facet joint (and very likely benign).

**Objective:** To determine the value of using SPECT/CT in addition to planar imaging or SPECT alone in the setting of prostate cancer.

**Methods:** 40 patients referred consecutively over 2 years for evaluation of metastatic prostate cancer were included in the study. All patients had a PSA >10 ng/mL, back pain, and/or a Gleason score of ≥7. All patients underwent both whole-body planar and directed SPECT/CT imaging. Images were interpreted by 2 experienced reviewers who rated findings as either benign, malignant, or equivocal. Planar, SPECT, and SPECT/CT were evaluated separately.

**Results:** A total of 50 areas of increased tracer uptake were seen in the 40 subjects. For planar imaging, 72% of the lesions were considered equivocal. For SPECT imaging, 50% of the lesions were categorized as equivocal. In contrast, only 8% of the lesions were determined to be equivocal with SPECT/CT. Six vertebral lesions from 5 patients were reclassified from malignant to benign or vice versa when SPECT/CT scans were reported, representing a change in diagnosis in 5 of 40 subjects (12.5%) in the study group. All of these findings were confirmed by follow-up as correct on SPECT/CT.

**Conclusions:** The addition of SPECT/CT to both SPECT and planar bone imaging leads to an improvement in diagnostic confidence for the presence or absence of metastases.

**Reviewer's Comments:** Here is another of multiple studies published in the past 2 to 3 years indicating the superiority of SPECT/CT for bone imaging of metastatic disease. However, I wonder if eventually this will all become moot if, as I suspect will be the case, F-18 PET/CT becomes the standard for skeletal imaging in the not too distant future? It appeared from the data presented that there were no additional lesions, benign or malignant, detected by SPECT not seen on planar images. This is surprising in a series of 40 subjects since it is well known that SPECT imaging enhances the sensitivity for skeletal abnormalities compared to planar imaging alone. Although accuracy calculations were not performed in this study, the correct change from benign to malignant or malignant to benign in the 5 patients supports an improved sensitivity and specificity for SPECT/CT over planar imaging. (Reviewer-David Bushnell, MD).

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Keywords: SPECT/CT, Prostate Metastases

Print Tag: Refer to original journal article
In Vivo Imaging of Macrophage Activity in Coronary Arteries

In Vivo Imaging of Macrophage Activity in the Coronary Arteries Using 68Ga-DOTATATE PET/CT: Correlation With Coronary Calcium Burden and Risk Factors.

Rominger A, Saam T, et al:

J Nucl Med 2010; 51 (February): 193-197

Ga-68 DOTATATE shows increased uptake in calcified atherosclerotic plaques in the coronary arteries.

**Background:** Vulnerable coronary plaques tend to concentrate white blood cells, primarily macrophages. Macrophages have been shown to express somatostatin receptors. PET/CT can be used to image the somatostatin receptor ligand 68Ga-[1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid]-D-Phe1,Tyr3-octreotate (DOTATATE).

**Objective:** To correlate the uptake of Ga-68 DOTATATE with the presence of calcified plaques and cardiac risk factors.

**Design:** Prospective cohort study.

**Participants:** 70 consecutive patients referred for a contrast-enhanced PET/CT scan because of the presence of a neuroendocrine tumor.

**Methods:** Patients were injected with 3 MBq/kg of Ga-68 DOTATATE for a contrast-enhanced PET/CT. A target-to-background ratio was measured in the left anterior descending coronary artery (LAD), and CT images were used to detect calcified plaque. Cardiovascular risk factors and cardiac history were recorded.

**Results:** Ga-68 DOTATATE uptake was present in the LAD of all patients. The target-to-background ratio in the LAD correlated significantly with the presence of calcified plaque ($R^2 = 0.34; P < 0.01$), prior vascular events ($R = 0.26; P < 0.05$), and male sex ($R = 0.39; P < 0.05$).

**Conclusions:** In a series of oncologic patients, increased Ga-68 DOTATATE in the LAD corresponded to the presence of calcified plaques and increased cardiovascular risk factors.

**Reviewer's Comments:** This study did not look at clinical outcomes. The relatively weak correlation between Ga-68 DOTATATE uptake and calcified plaque ($R = 0.34$) may mean that the agent doesn't work very well or, alternatively, that it provides important complementary information (i.e., a weak correlation suggests that the 2 imaging methods are measuring different things). We need outcome studies to know for sure. However, this paper highlights the importance of closely evaluating the heart when performing Ga-68 DOTATATE scanning. Of note, Ga-68 DOTATATE has an advantage in cardiac imaging over FDG since the myocardium in this study was consistently devoid of DOTATATE uptake whereas myocardial uptake of FDG is unpredictable.

(Reviewer-Thomas F. Heston, MD).

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Keywords: Atherosclerosis, Plaque Imaging, 68Ga-DOTATATE PET/CT

Print Tag: Refer to original journal article
Sestamibi Is Sensitive for Postsurgical Evaluation of DTC

Clinical Usefulness of 99mTc-MIBI Scintigraphy in the Postsurgical Evaluation of Patients With Differentiated Thyroid Cancer.

Campenni A, Violi MA, et al:

Nucl Med Commun 2010; January 16 (): epub ahead of print

Tc-99m sestamibi has a high sensitivity for the detection of metastatic disease in differentiated thyroid cancer and may be useful in the postsurgical setting to help determine optimal management.

**Background:** Differentiated thyroid cancers (DTC) are among the most curable neoplasms. Initial treatment typically consists of surgical excision with subsequent ablative radioiodine therapy. Determining the ideal dose of radioiodine therapy depends on the burden of remaining tissue. One meta-analysis has shown that one-fourth of all recurrences and metastases do not concentrate radioiodine.

**Objective:** To investigate the potential utility of Tc-MIBI in the postsurgical follow-up of patients with DTC.

**Design:** Prospective cohort.

**Participants:** 82 consecutive patients with DTC (61 women, 21 men) referred for postsurgical evaluation for radioiodine therapy.

**Methods:** Patients were studied after total or near-total thyroidectomy no earlier than 3 months after thyroidectomy and before any radioiodine therapy. All patients underwent Tc-MIBI scanning when in a euthyroid state with a suppressed TSH. Patients remained on levothyroxine during Tc-MIBI scanning. All patients subsequently underwent radioiodine therapy and scanning after being off of T4 for 5 weeks. Thyroglobulin levels were also recorded.

**Results:** Tc-MIBI detected thyroid remnants in 53 of 82 patients (65%) and metastatic foci in 10 of 11 (91%) patients (using the radioiodine scan as the gold standard). One patient with metastatic disease had false-negative results by Tc-MIBI and radioiodine. Tc-MIBI was as sensitive for the detection of metastatic DTC as the postsurgical 1110 MBq radioiodine scan.

**Conclusions:** Tc-MIBI has a high sensitivity for the detection of metastatic lesions from DTC.

**Reviewer's Comments:** This study also highlights the importance of carefully evaluating the raw data when performing Tc-99m sestamibi myocardial perfusion imaging. The authors conclude that Tc-MIBI imaging prior to radioiodine therapy can help determine dose and whether additional surgical intervention is necessary. (Reviewer-Thomas F. Heston, MD).

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Keywords: Differentiated Thyroid Cancer, Iodine-131, Metastatic Disease, 99mTc-MIBI Scan, Thyroid Imaging

Print Tag: Refer to original journal article
**Background:** The large majority of the peer-reviewed literature supports the concept that an abnormal gallbladder ejection fraction (GBEF) can predict pain response to cholecystectomy. However, there have been some challenges to this premise. The authors of this paper believe that part of the problem resides in the lack of standardized protocol and corresponding normal limits for assessing GBEF.

**Objective:** Consequently, the goal of this research was to determine the optimal method for determining GBEF.

**Methods:** Using Tc-99m mebrofenin, the authors studied 60 normal volunteers using 3 distinct infusion rates (15, 30, and 60 minutes) for cholecystokinin in a dosage of 0.02 μg/kg. Each exam was performed on a separate day. The coefficient of variation (CV) was calculated for GBEF for each of the 3 infusion rates.

**Results:** The authors reported that the lowest CV was found with the 60-minute infusion with a value of 19%. The 30- and 15-minute infusions led to a CV of 35% and 52%, respectively. The differences were all statistically significant. For the 60-minute infusion, 95% of the subjects demonstrated a GBEF of ≥49%, and 99% of the subjects demonstrated a GBEF of ≥38%. For the 30-minute infusion, the authors reported that 95% of the GBEFs were >18%, and 99% of the GBEFs were >12%. Standard deviations, although calculated, were not used to determine the lower limits of normal because the data did not demonstrate a Gaussian distribution.

**Conclusions:** A 60-minute infusion of sincalide should become the standard for calculating GBEF, and the lower limit of normal for this value should be set at 38% with this infusion rate.

**Reviewer's Comments:** Perhaps this approach recommended by the authors would improve the accuracy by which GBEF discriminates surgical responders from non-responders. By the way, looking at their data and using 2 standard deviations below the mean as the normal cut-off for a 30-minute infusion (which is what most of us currently use) leads to a lower limit of normal of 23% for GBEF. This may be important since many centers seem to accept a lower limit of normal of 35%. (Reviewer-David Bushnell, MD).

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Keywords: Gallbladder Ejection Fraction

Print Tag: Refer to original journal article
The noise equivalent count rate is a measure of data quality that includes the increased variation associated with corrections for dead-time, scatter, and random coincidences.

**Background:** The number of acquired events in PET imaging has a strong and potentially non-linear dependence on body weight. Recognition of this fact can lead to a more sensible dosing regimen for pediatric PET imaging.

**Objective:** To develop a quantitative pediatric dosing protocol for clinical PET imaging.

**Methods:** The noise equivalent count rate density (NECRD), which includes the effects of random and dead-time corrections, was used to investigate image data quality as a function of body size. Phantom measurements and patient studies were used to estimate individual NECRD curves. From this information, the reduction in administered activity or scan time to achieve similar results for a standard 70-kg adult was obtained. Quantitative expressions for the NECRD were formulated in terms of administered activity, body weight, and scan time. This was used to develop rules for pediatric imaging protocols. These rules were tested on a group of 73 patients ranging in weight from 11.5 to 91.4 kg. Comparisons were made to dosing protocols, which were based on patient body surface area, weight, or age.

**Results:** The NECRD approach correlated best with patient weight and yielded dosing estimates similar to those obtained with the method proposed by Clark in which the administered activity is scaled linearly by patient weight. This was true over most of the weight range except for newborns, in whom the NECRD approach yields dosing estimates that are 50% less. The expression for the amount of activity required to maintain a constant NECRD with a fixed imaging time was 14.8 \times \exp\left[0.046/\text{kg} \times \text{weight kg}\right] assuming a 1-hour uptake time.

**Conclusions:** The authors’ dosing approach based on NECRD provides rational estimates that yield constant data quality. If found to valid, substantial dose reductions for infants may be obtained compared to weight-based approaches.

**Reviewer’s Comments:** It is worthwhile to explore a scientific approach for determining how much activity to administer for PET and other nuclear medicine studies. It should be recognized, however, that the goal should be to have enough activity so that the probability is high that a diagnostic study is obtained. In that sense, approaches that underestimate the target dosing are more of an issue than those that overestimate the dosing. If a PET or other diagnostic study is indicated, the biggest risks to the patient and overall detriment to the delivery of health care is an inadequate study. (Reviewer-Mark T. Madsen, PhD).

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Keywords: PET, ALARA, Dose Optimization, 18F-FDG

Print Tag: Refer to original journal article
In response to reports of rising exposure to medical radiation in the U.S. population, in February 2010, the FDA announced an initiative to reduce unnecessary radiation exposure from CT, fluoroscopy, and nuclear medicine exams.

Radioactive decay results in the emission of electromagnetic energy in the form of gamma and x-ray photons, and/or particulate energy in the form of alpha and beta particles. The quantity of the radiopharmaceutical administered is most often specified by its activity in conventional units of millicuries (mCi), the quantity that gives rise to a decay rate of 37 million nuclear decays per second. Since one decay per second is also known in the System Internationale as a becquerel (Bq), one millicurie equals 37 million Bq, or 37 megabecquerel (MBq). Gamma rays and x-rays are both photons, i.e., electromagnetic (EM) radiation. Photons have neither mass nor charge. Gamma rays are emitted from within the nucleus. X-rays originate with the atomic electrons. If a beta emitter can be delivered close to the tumor, it will result in a larger dose to the diseased tissue than from typical gamma emitters, as well as less dose to other healthy tissues. In order to maximize the effectiveness of the treatment, beta emitters are used that have high energy emissions. For example, the maximum energy of an 89Sr beta particle (used for bone-pain palliation) is 1.5 MeV. For 90 Y (used with Zevalin in the treatment of non-Hodgkin's lymphoma), it is 2.3 MeV. As beta radiation passes through body tissue, secondary radiation is produced, termed bremsstrahlung. These are typically penetrating photons (x-rays). More bremsstrahlung radiation is produced in high atomic number materials (e.g., lead) than low Z materials (e.g., plastics). This is why plexiglass, rather than lead, is recommended for shielding a high energy beta emitter. A nucleus can decay by electron capture, as an orbital electron combines with a proton in the nucleus, transforming it into a neutron. X-rays are produced when the vacancy left by the captured electron is filled by another (outer) electron; 201 Tl is an example of such a nucleus. Thallium decays to 201 Hg (mercury). We image primarily mercury x-rays (about 70 keV) and a small percentage of gamma rays (167 keV) arising from de-excitation of excited nuclear states of 201 Hg.

**Reviewer's Comments:** In response to reports of increasing exposure to medical radiation in the U.S. population, in February 2010, the Food and Drug Administration (FDA) announced an initiative to reduce unnecessary radiation exposure from CT, fluoroscopy, and nuclear medicine exams. The FDA plans to regulate medical imaging devices and will also collaborate with other federal agencies and health care professional groups. The FDA also announced that it intends to hold a public meeting to solicit input on requirements in connection with the initiative. The FDA's initiative came as the U.S. House of Representatives is preparing to hold hearings on the issue of medical radiation. (Reviewer-).
New Respiratory Gating Technique Lets PET Patients Breathe Easy

Implementation of an Automated Respiratory Amplitude Gating Technique for PET/CT: Clinical Evaluation.
Chang G, Chang T, et al:


Dividing the respiratory cycle into time bins (phase gating) rarely works because irregular breathing is common. Gating based on the magnitude of inspiration or expiration is shown to be practical.

**Background:** Respiratory motion degrades PET scans, but available methods to compensate for this require 4D CT or specific breathing maneuvers by the patient.

**Objective:** To describe and evaluate a new method for respiratory gating of PET studies that does not require additional CT scans or patient breathing tasks. Gating is performed on the basis of the amplitude of the inspiration or expiration.

**Methods:** During the CT scan acquired over the thorax, patients are asked to breathe normally while an electronic device monitors the amplitude of the respiratory motion. The PET study of the corresponding area is acquired in list mode along with trigger signals that indicate when the patient respiratory motion falls into the range associated with the respiratory amplitude of the CT scan. For the gated amplitude technique, only the triggered portion of the acquisition is included in the reconstruction. This portion of the PET study was integrated into the rest of the PET whole-body study. The technique was tested on a total of 13 patients with a total of 21 thoracic tumors referred for PET imaging. Comparisons of mean and max SUVs along with the signal-to-noise ratios and volumes of each lesion were made between the amplitude-gated and the ungated reconstructed images.

**Results:** The gated amplitude technique was successfully applied on each subject. On average, there was a >25% increase in the mean and max SUV with application of the gated amplitude technique. There was also a similar increase in the average lesion signal-to-noise ratio, while the average lesion volume decreased by 37%. While some individual lesions showed little change in SUV, others exceeded 60%.

**Conclusions:** The respiratory amplitude gating technique is feasible on current PET/CT scanners that support list mode acquisition. The authors note that its implementation does not increase patient radiation dose and does not require patient breath control actions.

**Reviewer’s Comments:** This is an interesting approach that appears to have merit in the absence of more sophisticated approaches. The primary limitation is the increased PET acquisition time, since events acquired outside of the amplitude triggers are ignored. In this investigation, this caused an increase of about 7 minutes, which is probably tolerable. However, there may be times when the breathing amplitudes during the CT study fail to be reproduced. These situations will probably result in a retake scan. (Reviewer-Mark T. Madsen, PhD).

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Keywords: Amplitude Gating, PET/CT, Automation

Print Tag: Refer to original journal article
A statistically significant change in the SUV of 18F-fluoride PET measured at the lumbar spine and hip has been reported that parallels variations in serum markers of bone formation and resorption.

The most widely used method for assessing bone strength is the measurement of biochemical serum or urine markers. These portray prompt response to treatment with an anti-resorptive agent such as a bisphosphonate. Bone resorption markers decline within a month. Bone formation markers, however, show no response at 4 weeks but decline around 3 months. However, biochemical changes may be distorted by daily and hourly variations in the measurements. Dual-energy x-ray absorptiometry (DEXA) monitors changes in bone mineral density, but several years may be needed to detect changes. Degenerative disease complicates interpretation and, with bisphosphonates, part of the bone mineral density increase is caused by the increased secondary mineralization of newly formed bone tissue associated with the longer remodeling cycle. Strontium ranelate treatment results in large mineral density changes when measured by DEXA, but these are actually artifactual increases caused by replacement of calcium atoms in bone by strontium, which attenuates x-rays more strongly. As an alternative to DEXA, 18F-fluoride has the advantage of quantitative studies performed at the spine or hip. Significant correlations have been observed between regional skeletal uptake of 18F-fluoride PET and bone mineral apposition rate. 18F-fluoride PET has been used to assess therapeutic response in metabolic bone disease. 18F-fluoride PET also can assess neovascularization after allogenic bone grafting, periprosthetic bone formation after joint replacement, and fracture healing. Quantitative radionuclide studies of bone measure regional skeletal uptake as a percentage of injected dose or measure of plasma clearance from the time-activity curve in the selected region of interest and the blood input curve. SUV to quantify PET 18F-fluoride studies is much easier to obtain than plasma clearance data, which require a 60-minute dynamic PET acquisition together with continuous blood sampling. The same choice between measuring uptake or plasma clearance also exists for 99mTc-MDP. These quantitative radionuclide studies now have a well-established role in research, but the challenge remains of developing and validating simpler methods that may have wider clinical use.

Reviewer’s Comments: This editorial/update article was inspired by a paper in the November 2009 issue of the *Journal of Nuclear Medicine* by Uchida and colleagues. In a prospective study, the authors demonstrated the utility of quantifying bone turnover using 18F-fluoride SUV at the lumbar spine and femoral neck. They found a statistically significant change in SUV that paralleled variations in serum markers of bone formation and resorption. This sounds great, but PET seems to be an expensive way to assess response to treatment for osteoporosis. Tc-99m MDP may be worth a similar trial. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Bone, Quantitative Studies

Print Tag: Refer to original journal article
Bremsstrahlung images are generally inferior to gamma ray images because of the large energy windows (60%) that have substantial scatter and collimator penetration components.

**Background:** Y-90 therapy for lymphoma and other cancers is available. Performing treatment planning with this tracer through bremsstrahlung imaging would have many advantages.

**Objective:** To evaluate conjugate-view whole-body bremsstrahlung imaging for estimating tissue and organ radiation doses resulting from therapeutic administrations of Y-90 labeled radiotracers.

**Methods:** Experiments were performed using a physical torso phantom with a liver insert along with Monte Carlo simulations for 70-kg and 95-kg subjects. The physical whole-body bremsstrahlung anterior and posterior studies were acquired on a GE SPECT CT along with a scout view for attenuation correction. That system was also modeled for simulation experiments. High-energy collimators were used, and the energy peak was centered at 150 keV with a 60% window. For the physical measurement, 780 MBq of Y-90 was uniformly distributed in the liver insert, with no other radioactivity present in other compartments. The NCAT digital phantom was used to generate the radioactivity distributions in the liver, kidneys, spleen, and generalized body background. A standard Monte Carlo routine (SIMIND) was used to generate the simulated whole-body conjugate views. Resolution recovery processing was used to compensate for scattered radiation and collimator penetration based on simulated point response functions at different source depths. Region counts were determined from the processed images, and organ activities were calculated from the geometric mean using the standard corrections for attenuation obtained from the CT scout views and camera activity calibrations.

**Results:** Without the resolution recovery processing, the organ activities were underestimated by >50% in both the physical phantom and simulation studies. When it was applied, the liver activity was underestimated by 15% in the physical measurements and by 11% in the simulations. In both cases, the total body activity was overestimated by 26% and 20%, respectively. The Poisson noise level did not have any significant effect on the quantification or the image quality.

**Conclusions:** Y-90 activity in organ ROIs can be quantified with reasonable accuracy when proper compensation for scatter and collimator penetration are used.

**Reviewer's Comments:** Although the authors make good use of resolution recovery software and obtain reasonably good results for their physical phantom and simulations, their results really apply only to the measurements they made and cannot be assumed to cover the range of imaging situations. It seems likely that errors on the order of a factor of 2 larger than those found in this study are not only possible, but are also likely because of uncertainties in the body remainder activities and more extreme problems with overlapping organs. In my opinion, SPECT imaging offers a much more consistent and accurate approach to internal radiation dose estimates including bremsstrahlung imaging. (Reviewer-Mark T. Madsen, PhD).

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Keywords: Bremsstrahlung Imaging, Internal Dosimetry, Radionuclide Treatment Planning

Print Tag: Refer to original journal article
When Is Imaging With C-11 PET-CT Useful?


Giovacchini G, Picchio M, et al:

Eur J Nucl Med Mol Imaging 2010; 37 (): 301-309

Age, advanced disease stage, and prior biochemical failure are independent predictors of a positive C-11 PET/CT scan.

**Objective:** To identify risk factors other than rising PSA that are predictive of a positive C-11 choline PET/CT.

**Background:** Prostatectomy is considered curative in prostate cancer patients. However, up to 80% of patients subsequently develop biochemical failure (ie, increasing PSA) within 5 years of resection, indicating recurrence. Although C-11 PET/CT has been shown to be useful in detecting recurrence in this population, it is unclear when these patients should undergo C-11 imaging, as no threshold PSA value has been established. As such, this study aims to identify other factors predictive of a positive C-11 PET/CT in order to establish which patients would benefit from C-11 imaging.

**Design/Methods:** This retrospective study evaluated 358 patients who underwent prostatectomy for prostate cancer, with subsequent development of biochemical failure. Patients underwent C-11 PET/CT imaging. All patients were followed up for at least 2 years, with validation of PET/CT findings done in the majority of those with clinical follow-up (only 13% had histopathological confirmation). Univariate and multivariate analyses were performed to evaluate various factors in predicting a positive C-11 PET/CT. ROC analysis was also done to determine the optimal cut-off PSA level in distinguishing a positive C-11 PET/CT from a negative one.

**Results:** The overall rates of sensitivity, specificity, positive predictive value, and negative predictive value of C-11 PET/CT in detecting recurrence were 85%, 93%, 91%, and 87%, respectively, when validated using clinical follow-up and histopathology (87% vs 13%). Increasing PSA level was an independent predictor of scan positivity, with 82% of patients with PSA levels >3 ng/mL demonstrating positive scans (vs only 19% of those with PSA levels between 0.2 and 1.0 ng/mL). Increasing age, prior biochemical failure, and higher disease stage were also independent predictors of a positive scan. Higher Gleason scores, use of androgen deprivation therapy, and time to trigger PSA were not predictive of scan positivity when included in the multivariate analysis. The ROC demonstrated the optimum PSA in distinguishing positive from negative scans to be 1.4 ng/mL, yielding a sensitivity and specificity of 73% and 72%, respectively.

**Conclusions:** When deciding whether to refer patients for C-11 PET/CT imaging, higher PSA values (>3 ng/mL), age, advanced-stage disease, and previous biochemical failure are all independent predictive factors of a positive scan and should be considered.

**Reviewer's Comments:** Interesting study that looks at other factors that may be useful as predictors of a positive C-11 PET/CT, other than elevated PSA levels. The authors point out that rising PSA levels don't adequately reflect scan positivity in that an optimal level hasn't been established at which C-11 PET/CT imaging is useful. This suggests that imaging can be negative even when the levels are abnormal. As such, this study provides useful information, demonstrating that other factors should be considered when determining whether imaging with C-11 PET/CT would be useful. (Reviewer-Damita Thomas, MD).

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Keywords: Prostate Cancer, C-11 Choline PET/CT, Predictive Factors

Print Tag: Refer to original journal article
Cardiac CT angiography has been shown to be particularly useful to rule out significant coronary artery disease; a negative scan has a very favorable prognosis.

**Background:** Multislice computed tomography (MSCT) technology has developed rapidly over the past few years, which has allowed the high-resolution, noninvasive imaging of the coronary arteries and surrounding structures.

**Objective:** To provide a review of the medical literature and address the clinical utility of cardiac MSCT.

**Methods:** Literature review.

**Results:** Since the introduction of MSCT, improvements have decreased acquisition time, increased detector number, and increased spatial and temporal resolution. CT angiography (CTA) currently has excellent image quality that has resulted in a high diagnostic accuracy in the detection of coronary artery disease (CAD). More recent developments in MSCT technology have focused on reduction of the radiation dose. Drastic reductions in patient radiation dose have resulted from dose modulation and prospective ECG gating. With the introduction of 320-slice MSCT, volumetric scanning of the entire heart is now possible in a single beat, reducing artifacts and increasing the percentage of patients eligible for scanning. CTA is particularly effective in the evaluation of suspected CAD, where a negative scan carries a very favorable prognostic value. MSCT can also be helpful in determining stent patency. MSCT is beginning to be used more frequently for the evaluation of cardiac function and myocardial perfusion as well.

**Conclusions:** A primary role of cardiac CTA appears to be in the usefulness of a negative scan. In these patients, the subsequent cardiac event rate is very low.

**Reviewer’s Comments:** Staying up to date with developments in cardiac CT angiography is important for nuclear physicians for at least a couple of reasons. First, nuclear medicine physicians are eligible to get Level II trained in cardiac CT according to criteria established by the American College of Cardiology and the American Society of Nuclear Cardiology. Secondly, as the growth of fused imaging grows, more and more myocardial perfusion scans are likely to include diagnostic quality CT imaging, which nuclear physicians will be expected to interpret. (Reviewer-Thomas F. Heston, MD).

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Keywords: Multislice CT, Imaging, Coronary Artery Disease

Print Tag: Refer to original journal article
Major advances in cardiac imaging have occurred across all modalities. Fused imaging is becoming commonplace.

**Background:** Cardiac imaging has undergone dramatic advances over the last decade, which has resulted in a rapid rise in the amount of money being spent on imaging. In the current economic climate, future imaging techniques must be thoroughly validated before they can expect insurance companies to cover the costs.

**Objective:** This article is a review of current cardiac imaging modalities (with the exception of echocardiography), with an emphasis on speculating on future directions for the modalities over the next 5 to 10 years. **Radionuclide Imaging:** Quantitation has been shown to improve the accuracy of imaging studies. It is anticipated that quantitation will become more common in assessing absolute myocardial blood flow and flow reserve. A new F-18 labeled myocardial perfusion agent (BMS-747158-02), which targets mitochondria, will allow exercise stress cardiac PET. This newer agent has a better myocardial extraction fraction than Tc-99m sestamibi or tetrofosmin. Newer gamma cameras may also eventually be able to quantitate blood flow. Fused imaging continues to grow allowing simultaneous function and structure evaluation (primarily calcium scoring). BMIPP shows good promise for advancing gamma imaging of ischemic memory. MIBG also is likely to see increased utilization for neuronal innervation. **Cardiac CT:** Major utility is in coronary calcium scoring. The role of CT angiography (CTA) is still undefined. CTA is good for low-risk patients, but these patients can also be effectively risk stratified using existing technology. The future of CT appears to be in its increasing ability to simultaneously evaluate the coronary arteries, ventricular function, valves, and myocardial perfusion; however, this technology is not fully developed or proven. **Cardiac MRI:** Contrast enhancement and stronger magnetic fields will drive developments in MR. With field strengths up to 7T, MR spectroscopy will permit noninvasive investigation of myocardial metabolism and biochemical alterations in vivo by imaging phosphorus-31, hydrogen-1, and sodium-23.

**Reviewer's Comments:** This review by Dr. George Beller provides an excellent overview of the various cardiac imaging modalities and areas of potential growth. As always, Dr. Beller provides the key information relevant for the clinical practice of cardiac imaging. He highlights the growing usefulness of fused imaging, necessitating the ability by physician readers to be able to evaluate multimodality images. (Reviewer-Thomas F. Heston, MD).

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Keywords: Cardiovascular Imaging, CT, MRI

Print Tag: Refer to original journal article
Although the PPV of PET/CT in patients with TB is lower, PET/CT still has high enough accuracy to be used in preoperative evaluation of lung cancer in TB endemic areas.

**Background:** The positive predictive value (PPV) of FDG PET/CT for assessing mediastinal lymph nodes in lung cancer staging is compromised in the setting of granulomatous disease. Lung cancer is the leading cause of cancer death worldwide, but staging with PET/CT may be more challenging in regions with endemic tuberculosis (TB).

**Objective:** To determine the accuracy of preoperative PET/CT for mediastinal lymph node staging of lung cancer patients in Hong Kong.

**Design/Participants:** This retrospective cohort study included all patients who underwent PET/CT prior to surgery with curative intent for non-small cell lung cancer from January 2003 to January 2006.

**Methods:** Patients who received preoperative chemotherapy or radiotherapy, patients with known previous or current metastatic lung cancer, and patients with histologically proven lung metastases from an extrapulmonary source were excluded. Patients that did not undergo mediastinal lymph node biopsy during surgery or mediastinoscopy were also excluded. A standardized uptake value ≥2.5 plus the radiologist's report were used to indicate the presence of abnormal mediastinal nodal uptake. For each mediastinal lymph node, the sensitivity and specificity of PET/CT were determined by comparison with histology.

**Results:** By comparing PET/CT with histology in all mediastinal and hilar lymph nodes sampled (n=249), PET/CT sensitivity, specificity, and accuracy were 35%, 84%, and 74%, respectively. The PPV and negative predictive value were 37% and 83%, respectively. Active TB, a history of TB, or radiological evidence of previous TB was present in 36% of the patients in this study (38/107). PPV was 39% in TB patients and 50% in non-TB patients.

**Conclusions:** PET/CT has a lower PPV for mediastinal staging in lung cancer patients with TB, but the accuracy of PET/CT is still high enough for routine preoperative evaluation of lung cancer patients in TB-endemic regions.

**Reviewer's Comments:** All patients in this study were surgical candidates, so there may have been some bias toward lower stage disease, which may partially explain the difference in sensitivity in this study compared to that in previous studies. (Reviewer-Shayne Squires, MD).

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Keywords: Lung Cancer, Mediastinum, Tuberculosis, PET

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Feasibility of FDG PET/CT to Monitor the Response of Axillary Lymph Node Metastases to Neoadjuvant Chemotherapy in Breast Cancer Patients.

Straver ME, Aukema TS, et al:
Eur J Nucl Med Mol Imaging 2010; February 4 (): epub ahead of print

The sensitivity of PET/CT for axillary metastases is good in breast cancer patients who are candidates for neoadjuvant therapy.

Background: Neoadjuvant chemotherapy for breast cancer can result in reducing inoperable disease to operable disease. The ability to monitor the response to neoadjuvant therapy would enable oncologists to modify therapy if response is less than optimal.

Objective: To determine the accuracy of FDG PET in detecting breast cancer axillary lymph node metastases in patients that will undergo neoadjuvant chemotherapy.

Participants/Methods: Study subjects were women with breast tumors >3 cm in diameter and/or at least 1 tumor-positive axillary lymph node. Positive lymph nodes were identified by axillary ultrasound and fine-needle aspiration (FNA) or by sentinel lymph node biopsy (SNB). Patients were scheduled to undergo neoadjuvant chemotherapy, prior to which FDG PET/CT imaging was performed. The accuracy of PET for identifying lymph node metastases was determined by comparison with the results of FNA or SNB.

Results: The presence of axillary node metastases was confirmed in 30 patients, of whom 29 were positive by PET/CT (sensitivity, 97%). In another 5 patients, no tumor was detected after FNA or SNB. One of these patients was excluded from further analysis because a follow-up PET/CT scan suggested that suspicious axillary lymph nodes were missed during sentinel node dissection. So altogether, there were 4 patients without detectable axillary metastases, all of whom were also negative by PET/CT (specificity, 100%). The maximum standardized uptake value of primary tumor compared to its corresponding lymph node metastases was not significantly different. The tumor-to-background ratio was higher for metastatic axillary nodes than for the primary tumor, presumably due to background breast activity. Primary tumors and axillary metastases that were triple negative showed higher PET activity than estrogen receptor-positive or HER2-positive tumors.

Conclusions: In breast cancer patients scheduled to undergo neoadjuvant chemotherapy, FDG PET/CT imaging can be used to detect axillary lymph node metastases. This suggests potential feasibility for monitoring response to neoadjuvant therapy.

Reviewer's Comments: In this study, the sensitivity of PET/CT for detecting lymph node metastases in patients who are scheduled to undergo neoadjuvant chemotherapy was high, but this result does not necessarily apply to a lower risk population of patients. Specificity also appeared high, but there were only 4 negative patients. Nevertheless, the high sensitivity in this population supports the authors' conclusion that PET may potentially be used to assess response to neoadjuvant therapy in axillary lymph nodes. (Reviewer-Shayne Squires, MD).

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Keywords: Breast Cancer, Neoadjuvant Therapy, PET

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F-18-FDOPA is a better imaging agent than FDG for low-grade gliomas because of its low background activity in the brain.

**Background:** Low-grade gliomas are difficult to detect using F-18 FDG as radiotracer due to modest FDG uptake and high background FDG activity in the brain. F-18-FDOPA and F-18 FLT, alternative PET tracers for malignancy, may work better.

**Objective:** To compare imaging with FDG, FDOPA, and FLT in PET/CT imaging of primary and recurrent low-grade gliomas.

**Participants/Methods:** The study included 15 patients with newly diagnosed or previously treated low-grade glioma. Each glioma in the study was grade I or II by World Health Organization histopathologic classification. Three patients had newly diagnosed glioma, and 10 had suspected recurrent disease. Two patients without progression for 2 years by MRI and clinical follow-up served as negative controls. The 3 patients with newly diagnosed disease underwent surgical resection after PET. Ten patients with suspected recurrence underwent biopsy, which was positive in 9. The 2 control patients and 1 biopsy-negative patient were followed for 20 months. Each patient underwent PET/CT imaging with F-18-FDOPA, F-18 FDG, and F-18 FLT. Each patient was also imaged by MRI; 12 patients were imaged by MR spectroscopy. Images were interpreted as abnormal if there was tracer uptake higher than background. Background was defined as the area immediately adjacent to tumor.

**Results:** Using FDOPA, all 3 primary and 9 recurrent gliomas were well visualized. The patient with suspected recurrence that was negative by FDOPA had a negative biopsy and no evidence of recurrence at follow-up. The 2 negative control patients were negative by FDOPA. Using FDG, 1 primary and 6 recurrent tumors were visualized, but the extent of visualization and delineation was poorer than with FDOPA. The 2 control patients were negative by FDG. Five patients who were negative by FDG were positive by FDOPA. Using FLT, 1 primary and 3 recurrent tumors were well visualized. The difference in average maximum standardized uptake value (SUV) for each of the 3 tracers was statistically significant, with FDG having the highest SUV and FLT having the lowest.

**Conclusions:** F-18-FDOPA is an ideal agent for imaging primary or recurrent low-grade glioma.

**Reviewer’s Comments:** Tumor FDG uptake was actually higher than FDOPA, but because of the high background uptake of FDG by the cerebral cortex, FDOPA performed better in this study. (Reviewer-Shayne Squires, MD).

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Keywords: Glioma, PET, FDOPA

Print Tag: Refer to original journal article
The rate of incidentally detected focal thyroid FDG uptake is low, but the likelihood of malignancy in such instances is high enough to warrant biopsy.

**Background:** Incidental focal FDG uptake in the thyroid of patients undergoing PET/CT for nonthyroid cancer has been shown to carry a significant risk of thyroid malignancy. Previous studies included mostly older patients at relatively higher risk of thyroid malignancy who had concurrent illness. The significance of thyroid incidentalomas in young, healthy subjects has not been previously reported.

**Objective:** To evaluate the significance of incidental focal uptake of FDG in the thyroid gland of young, healthy volunteers.

**Participants/Methods:** At the Hamamatsu Medical Imaging Center in Japan, a cohort of healthy volunteers were studied with FDG PET under several research protocols, including one investigating the use of whole-body FDG-PET for cancer screening. Subjects with a past history of cancer or thyroid surgery were excluded. Subjects with focal accumulation of FDG in the thyroid underwent further evaluation with ultrasound and fine-needle aspiration biopsy (FNAB).

**Results:** During the study period, 1529 people underwent PET scanning, and 20 with focal FDG uptake in the thyroid met inclusion criteria. The mean subject age was 46.5 ± 9.5 years. Histopathology demonstrated malignancy in 11 cases, benignity in 8, and indeterminacy in 1. There was no significant difference in maximum standardized uptake value or nodule size by ultrasound in subjects with malignant nodules versus subjects with benign nodules.

**Conclusions:** Focal FDG uptake in the thyroid gland in patients undergoing PET/CT for nonthyroid cancer carries a relatively high risk of thyroid malignancy.

**Reviewer's Comments:** The results of this study suggest that the risk of thyroid malignancy associated with focal FDG thyroid uptake in young, healthy subjects is similar to that seen in older patients with higher pretest probability of thyroid cancer. This study suffers from the same limitations as other similar studies with regard to low numbers, but together, the various studies are in broad agreement that focal thyroid PET activity warrants further evaluation. (Reviewer-Shayne Squires, MD).

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Keywords: FDG-PET, Thyroid Cancer, Incidentalomas

Print Tag: Refer to original journal article
Incidentally detected focal FDG uptake in the breast is more likely benign than malignant, but the rate of malignancy is high enough to justify further evaluation.

Objective: To evaluate the significance of incidental breast findings on FDG-PET in patients being evaluated for nonbreast malignancy.

Design/Participants: This retrospective study included patients who underwent PET/CT scanning with FDG for nonbreast malignancy between March, 2000 and June, 2007.

Methods: Subjects were included if there was a report of abnormal FDG focus in the breast, axilla, or chest wall with a reported standardized uptake value (SUV). Subjects were excluded if the FDG pattern in the breast was described as mild diffuse or likely physiologic. Subjects were also excluded for a known history of breast disease. Additional chart review was performed to document the maximum size and SUV of breast findings and the results of any follow-up diagnostic studies, including additional PET, MRI, mammogram, ultrasound, or tissue biopsy. Subjects were classified by status at last follow-up as having no disease, being dead with cause specified, or being alive with disease.

Results: During the study period, 45,000 PET scans were performed. Of these, 60 met inclusion criteria. Of these, additional work-up was performed in 40 patients, 12 of whom went on to have tissue biopsy. Seven of the 12 biopsies were positive for malignancy. In summary, 12% of the total population of patients with breast incidentaloma by PET/CT were shown to have breast malignancy. Some patients with incidental breast findings avoided biopsy for a variety reasons, including resolution of the abnormality on follow-up PET/CT, negative results by additional breast imaging with other modalities, or advanced malignancy of another organ system. Although the number of biopsy results was too small to achieve statistical significance, the mean SUV for patients with malignancy was 4.63, and the mean SUV in benign cases was 2.55.

Conclusions: The proportion of breast incidentalomas in patients undergoing PET/CT for nonbreast malignancy is small, but the rate of malignancy among incidentalomas is high enough to warrant further evaluation.

Reviewer's Comments: In this study, the most common reason for not pursuing further work-up in patients with breast incidentalomas was that there was metastatic disease on the PET/CT, indicating advanced stage of the index malignancy. (Reviewer-Shayne Squires, MD).

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Keywords: Incidentaloma, Breast Cancer, PET/CT

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Is SPECT-CT HBS Helpful in Assessing Liver Function, Volume?

99mTc-Mebrofenin Hepatobiliary Scintigraphy With SPECT for the Assessment of Hepatic Function and Liver Functional Volume Before Partial Hepatectomy.

de Graaf W, van Lienden KP, et al:

J Nucl Med 2010; 51 (February): 229-236

Hepatobiliary scintigraphy is a useful tool in the preoperative assessment of remnant liver function in patients undergoing partial hepatectomy.

**Background:** The preoperative evaluation of future remnant liver (FRL) function (ie, postoperative liver function) is essential in patients undergoing partial hepatectomy in that patients at high risk of developing liver failure postoperatively are identified and surgery is avoided. Although CT volumetry is the current diagnostic standard, it is only an indirect measure of liver function as only postoperative parenchymal volume is assessed without the benefit of the functional status of the remaining liver. As such, hepatobiliary scintigraphy (HBS), widely used to assess the functional status of the hepatobiliary system, is being evaluated as a tool to provide this information. Given SPECT/CT capabilities, its role to assess volume as well as functional status could supplant CT volumetry as the gold diagnostic standard.

**Objective:** To evaluate SPECT/CT hepatobiliary scintigraphy (HBS) in the assessment of liver function and volume.

**Design/Participants:** This retrospective study analyzed 36 patients who underwent CT volumetry and HBS with various parameters measured reflecting liver function and volume partial hepatectomy for clinically indicated reasons.

**Methods:** The patients were divided into 2 groups (normal vs abnormal liver parenchyma) based on histopathology from surgical specimens (with abnormal parenchyma defined as the presence of steatosis, cholestasis, fibrosis, or chronic inflammation). In half of the patients, a postoperative HBS was also done to determine the actual postoperative liver function.

**Results:** Of the 36 patients, 21 had abnormal parenchymal changes. The total liver function (TL-F) was significantly lower in patients with abnormal versus normal liver parenchyma, with the latter showing a slightly better correlation between FRL volume and FRL function. Among the 18 patients having a postoperative HBS, preoperative HBS showed a better correlation between actual postoperative liver function than did planar HBS and CT volumetry. Also, the %FRL-volume (FRL-V; a tool used to determine whether resection is feasible) was comparable to the %FRL-functional volume (FRL-FV) in patients with normal parenchyma but was significantly less than the %FRL-FV in patients with abnormal parenchyma. This suggests that the abnormal parenchyma had a greater impact on the functional volume of liver to be resected than on the liver that was to remain.

**Conclusions:** SPECT/CT HBS can provide a “complete and accurate prediction of postoperative remnant liver function.”

**Reviewer’s Comments:** This study highlighted the use of SPECT/CT HBS in the preoperative evaluation of partial hepatectomy patients, suggesting that it can possibly supplant CT volumetry as the gold standard, as it provides functional information in addition to accurately measuring remnant FRL volume. As expected, the study also showed that planar HBS over/underestimated function in patients undergoing right and left partial resection, respectively, when compared to function calculated from geometric mean count analysis emphasizing the need to perform this analysis when SPECT is not used. Although it is a relatively strong, albeit retrospective, study, it would have been strengthened if all patients had undergone postoperative SPECT/CT HBS and volumetry to compare preoperative and postoperative measurements. (Reviewer-Damita Thomas, MD).

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Keywords: Liver Function, CT Volumetry, Future Remnant Liver

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Individualized risk assessment of SPN may be possible using SUV and patient-specific pre-test probability factors for malignancy.

**Background:** Solitary pulmonary nodules (SPNs) present a diagnostic challenge in that conventional imaging often cannot discern malignant from benign lesions. FDG PET is widely used in the assessment of SPN, with both visual and quantitative standardized uptake value (SUV) assessment of glucose metabolism to evaluate for malignancy. Although several studies have shown the diagnostic and prognostic value of FDG PET in assessing SPN, the authors suggest that its role in the daily clinical management of patients with SPN is less defined. As such, 1 goal was to assess the role of FDG PET in the individualized risk stratification of patients with SPN.

**Objective:** To evaluate different SUV thresholds in determining malignancy of SPNs, to evaluate the prognostic value of SUVs, and to assess the individual risk of malignancy using the SUV and patients’ pre-test probability.

**Design/Participants:** This retrospective study evaluated 140 patients with SPN. All had FDG PET, with SPN visually and quantitatively assessed. The reference standard was histopathologic or 2-year follow-up. Sensitivity, specificity, positive/negative predictive values (P/NPV), and accuracy were calculated for both interpretative approaches. Survival analysis of SUV was also performed. Individual assessment of malignancy was calculated using the observed diagnostic parameters for each SUV threshold.

**Results:** Of the 140 patients, 80 had malignant SPNs and 60 had benign SPNs. Malignant SPNs had significantly higher SUVs than benign SPNs. Using visual interpretation, the sensitivity, specificity, and P/NPV were 94%, 70%, 81%, 89%, and 84%, respectively. SUV thresholds of 2.0, 2.5, and 4.0 were evaluated, with the latter showing the best diagnostic accuracy (sensitivity, specificity, P/NPV, and accuracy of 85%, 85%, 88%, 81%, 85%, respectively), reflecting the difficulty of choosing the optimal threshold SUV as there was overlap between malignant and benign lesions with SUVs ≤2.5. Patients with higher SUVs had significantly reduced survival rates.

**Conclusions:** Lower/higher SUV is associated with lower/higher malignancy risk, respectively. It may be possible to individualize the risk of malignancy using patient-based pre-test probability and SUV.

**Reviewer’s Comments:** The study echoes the known prognostic value and diagnostic accuracy of FDG PET in SPN assessment. The study also suggests that the risk of malignancy can be individualized. This comes with a caveat, as pointed out by the author, in that the individualized assessment is based on schema derived from their patient-based data. As such, these findings may not translate to study populations with varying pre-test probability factors or in centers that perform the PET study using a different uptake period (ie, 60, 90, 120 minutes). This study indirectly suggests that it may be possible to individually evaluate risk if based on center-specific prevalence and PET performance parameters. (Reviewer-Damita Thomas, MD).